REASONED OPINION

Review of the existing maximum residue levels (MRLs) for trinexapac according to Article 12 of Regulation (EC) No 396/2005[1]

European Food Safety Authority[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Trinexapac was included in Annex I to Directive 91/414/EEC on 01 May 2007, which is before the entry into force of Regulation (EC) No 396/2005 on 02 September 2008. EFSA is therefore required to provide a reasoned opinion on the review of the existing MRLs for that active substance in compliance with Article 12(2) of afore mentioned regulation. In order to collect the relevant pesticide residues data, EFSA asked the Netherlands, as the designated rapporteur Member State (RMS), to complete the Pesticide Residues Overview File (PROFile). The requested information was submitted to EFSA on 24 February 2009 and, after having considered several comments made by EFSA, the RMS provided on 04 November 2009 a revised PROFile.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC and the additional information provided by the RMS, EFSA issued on 09 August 2011 a draft reasoned opinion that was circulated to Member State experts for consultation. Comments received by 14 October 2011 were considered for finalisation of this reasoned opinion. The following conclusions are derived.

The toxicological profile of trinexapac was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI of 0.32 mg/kg bw/d. ADI was derived from studies carried out with trinexapac-ethyl but it may be applied to trinexapac. An ARfD was not deemed necessary for this active substance.

Primary crop metabolism of trinexapac was investigated following a single foliar application in wheat, rice and rape seed, hereby covering two different crop groups. Metabolic patterns in the different studies were shown to be similar and the relevant residue for enforcement and risk assessment in all plant commodities could be defined as the sum of trinexapac (acid) and its salts, expressed as trinexapac. A validated analytical method for enforcement of the proposed residue definitions is available, with an LOQ of 0.02 mg/kg in commodities with high water content and in dry commodities, and with an LOQ of 0.01 mg/kg in commodities with a high fat content.

[1] On request from EFSA, Question No EFSA-Q-2008-645, issued on 16 December 2011.

[2] Correspondence: pesticides.mrl@efsa.europa.eu

[3] Acknowledgement: EFSA wishes to thank the rapporteur Member State The Netherlands for the preparatory work on this scientific output.

Suggested citation: European Food Safety Authority; Review of the existing maximum residue levels (MRLs) for trinexapac according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2012;10(1):2511. [38 pp.] doi:10.2903/j.efsa.2012.2511. Available online: www.efsa.europa.eu/efsajournal

Regarding the magnitude of residues in all crops reported by the RMS, a sufficient number of supervised residues trials is available for barley, oats, rye, wheat and rape seed, which allowed EFSA to estimate the expected residue concentrations in the relevant plant commodities and to derive appropriate MRLs. For dry beans, EFSA was only able to derive a tentative MRL while for poppy seeds no residues trials were available and no MRL could be derived.

In processed commodities, trinexapac-ethyl were shown to be stable during pasteurisation, boiling, brewing, baking and sterilisation. A study conducted with trinexapac however showed that at the end of incubation, trinexapac had degraded and represented 51-59% of the total radioactivity and that two main metabolites are formed. One of them was not of toxicological concern but for the other metabolite the complete toxicology package has not been submitted. Nevertheless, based on the critical uses of trinexapac currently authorized within the EU, the overall chronic exposure represents less than 10% of the ADI and processing studies are not mandatory. Therefore further data are currently not considered essential. Studies investigating the magnitude of residues in processed commodities of barley and wheat and rye were also reported in the framework of the peer review but no robust processing factors for enforcement and risk assessment purposes could be derived from these studies. Further processing studies are currently not required as they are not expected to affect the outcome of the risk assessment. However, if there would be the intention from risk managers to derive more processing factors for enforcement purposes, additional processing studies might be required.

Occurrence of trinexapac residues in rotational crops was already investigated during the peer review of trinexapac. Confined rotational crop studies investigating the uptake of residues in lettuce, wheat, sugar beets and corn were reported. It was concluded that significant residues in rotational crops are not expected. These conclusions also apply to the GAPs of trinexapac supported in the framework of this review.

Based on the uses reported by the RMS, significant intakes were calculated for dairy ruminant, meat ruminants, poultry and pigs. Metabolism in poultry and lactating ruminants was sufficiently investigated and findings can be extrapolated to pigs as well. The relevant residue definition for both enforcement and risk assessment in poultry, ruminants and pigs was therefore defined as the sum of trinexapac (acid) and its salts, expressed as trinexapac. Based on the available livestock feeding study, it is also concluded that significant residues in edible matrices of ruminants, poultry and pigs are not expected and that MRLs for these commodities can be established at the LOQ, except for kidney where an MRL of 0.05 mg/kg is derived. A validated analytical method for enforcement of the proposed MRLs is available, with a LOQ of 0.01 mg/kg in animal tissues. For milk, the LOQ is proposed at 0.005 mg/kg.

Chronic consumer exposure resulting from the uses supported in the framework of this review was calculated and compared with the toxicological reference value derived for trinexapac. The highest chronic exposure was calculated for UK toddlers, representing 1.2% of the ADI. Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.

Based on the above assessment, EFSA does not recommend inclusion of this active substance in Annex IV to Regulation (EC) No 396/2005. MRL recommendations were derived in compliance with the decision tree reported in Appendix D (see table below for a summary). All MRL values listed as ‘Recommended’ in the table are sufficiently supported by data and therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL values listed in the table are not recommended for inclusion in Annex II because they require further consideration by risk managers (see table footnotes for details). In particular, certain tentative MRLs and existing EU MRLs still need to be confirmed by the following data:

- 4 additional residue trials supporting outdoor GAP on dry bean in southern and 4 additional residue trials in northern Europe;

- 4 residue trials supporting outdoor GAP on poppy seed in southern and 4 residue trials in northern Europe.

Moreover, in view of the future need to set MRLs in feed items, the following data might also be required:

- 4 residue trials supporting the northern GAP on grass;

If the above reported data gaps are not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level.

A minor deficiency was also identified in the assessment but this deficiency is not expected to impact either on the validity of the 'Recommended' MRLs or on the national authorisations. A confirmation that livestock feeding samples were stored in compliance with demonstrated storage conditions is therefore considered desirable but not essential.

Code number	Commodity	Existing EU MRL (mg/kg)	Outcome of the review	
			MRL (mg/kg)	Comment
Enforcement residue definition : sum of trinexapac (acid) and its salts, expressed as trinexapac				
300010	Beans (dry)	10	10	Further consideration needed[(a)]
401030	Poppy seed	0.05*	0.05	Further consideration needed[(b)]
401060	Rape seed	2	2	Recommended[(c)]
500010	Barley grain	0.5	0.5	
500050	Oats grain	0.5	0.5	
500070	Rye grain	0.5	0.5	
500090	Wheat grain	0.5	0.5	
1011010	Swine meat	0.05*	0.01*	
1011020	Swine fat (free of lean meat)	0.05*	0.01*	
1011030	Swine liver	0.05*	0.01*	
1011040	Swine kidney	0.05*	0.05	
1012010	Bovine meat	0.05*	0.01*	
1012020	Bovine fat	0.05*	0.01*	
1012030	Bovine liver	0.05*	0.01*	
1012040	Bovine kidney	0.05*	0.05	
1013010	Sheep meat	0.05*	0.01*	
1013020	Sheep fat	0.05*	0.01*	
1013030	Sheep liver	0.05*	0.01*	
1013040	Sheep kidney	0.05*	0.05	
1014010	Goat meat	0.05*	0.01*	
1014020	Goat fat	0.05*	0.01*	

Code number	Commodity	Existing EU MRL (mg/kg)	Outcome of the review	
			MRL (mg/kg)	Comment
1014030	Goat liver	0.05*	0.01*	
1014040	Goat kidney	0.05*	0.05	
1016010	Poultry meat	0.05*	0.01*	
1016020	Poultry fat	0.05*	0.01*	
1016030	Poultry liver	0.05*	0.01*	
1020010	Cattle milk	0.05*	0.005*	
1020020	Sheep milk	0.05*	0.005*	
1020030	Goat milk	0.05*	0.005*	
1030000	Birds' eggs	0.05*	0.01*	
-	Other products of plant and animal origin	See App. C	-	Further consideration needed (d)

(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.
(a): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers could be identified; no CXL is available (combination E-I in Appendix D).
(b): GAP evaluated at EU level is not supported by data but no risk to consumers could be identified for the existing EU MRL; no CXL is available (combination C-I in Appendix D).
(c): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination G-I in Appendix D).
(d): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either the specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix D).

KEY WORDS

trinexapac, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, plant growth regulator, trinexapac-ethyl.

TABLE OF CONTENTS

BACKGROUND

Regulation (EC) No 396/2005[4] establishes the rules governing the setting as well as the review of pesticide MRLs at European level. Article 12(2) of that regulation lays down that EFSA shall provide by 01 September 2009 a reasoned opinion on the review of the existing MRLs for all active substances included in Annex I to Directive 91/414/EEC[5] before 02 September 2008. As trinexapac was included in Annex I to the above mentioned directive on 01 May 2007, EFSA initiated the review of all existing MRLs for that active substance and a task with the reference number EFSA-Q-2008-645 was included in the EFSA Register of Questions.

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC. It should be noted, however, that in the framework of Directive 91/414/EEC only a few representative uses are evaluated while MRLs set out in Regulation (EC) No 396/2005 should accommodate for all uses authorised within the EU as well as uses authorised in third countries having a significant impact on international trade. The information included in the assessment report prepared under Directive 91/414/EEC is therefore insufficient for the assessment of all existing MRLs for a given active substance.

In order to have an overview on the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residue Overview File (PROFile). The PROFile is an electronic inventory of all pesticide residues data relevant to the risk assessment as well as the MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities and;
- the analytical methods for enforcement of the proposed MRLs.

The Netherlands, the designated rapporteur Member State (RMS) in the framework of Directive 91/414/EEC, was asked to complete the PROFile for trinexapac. The requested information was submitted to EFSA on 24 February 2009 and subsequently checked for completeness. On 04 November 2009, after having clarified some issues with EFSA, the RMS provided a revised PROFile.

A draft reasoned opinion was issued by EFSA on 09 August 2011 and submitted to Member States (MS) for commenting. All MS comments received by 14 October 2011 were considered by EFSA for finalization of the reasoned opinion.

[4] Commission Regulation (EC) No 396/2005 of 23 February 2005. OJ L 70, 16.3.2005, p. 1-16.
[5] Council Directive 91/414/EEC of 15 July 1991, OJ L 230, 19.8.1991, p. 1-32.

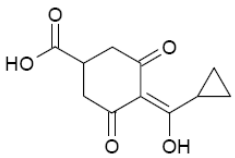
TERMS OF REFERENCE

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

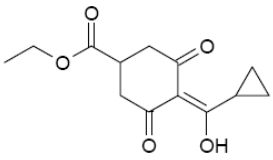
- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Trinexapac is the ISO common name for 4-(cyclopropyl-hydroxymethylene)-3,5-dioxo-cyclohexanecarboxylic acid (IUPAC) but it may be used as salts or esters. The ester variant that was used as a basis for the peer review of trinexapac under Directive 91/414/EEC is trinexapac-ethyl, ISO common name for 4-(cyclopropyl-hydroxymethylene)-3,5-dioxo-cyclohexanecarboxylic acid ethyl ester (IUPAC).



Trinexapac
(MW: 252.3)



Trinexapac-ethyl
(MW: 280.3)

Trinexapac and trinexapac-ethyl are unclassified plant growth regulator. Trinexapac-ethyl is taken up via leaves and shoots which results in morphological symptoms such as reduction of crop height or reduced elongation by inhibition of a certain step in the gibberellins biosynthesis.

Trinexapac was evaluated in the framework of Directive 91/414/EEC with The Netherlands being the designated rapporteur Member State (RMS). The representative uses supported for the peer review process were outdoor treatments of cereals, amenity turf and amenity grass-land at a rate of 0.2 kg a.s./ha for cereals and 0.4 kg a.s./ha for amenity turf and grass-land, both in northern and southern Europe. Following the peer review, which was carried out by EFSA, a decision on inclusion of the active substance in Annex I to Directive 91/414/EEC was published by means of Commission Directive 2006/64/EC[6], entering into force on 01 May 2007. According to Regulation (EU) No 540/2011[7], trinexapac is deemed to have been approved under Regulation (EC) No 1107/2009[8]. This approval is restricted to uses as plant growth regulator only.

The EU MRLs for trinexapac are established in Annexes IIIB of Regulation (EC) No 396/2005. All existing EU MRLs, which are established for the parent compound only are summarized in Appendix C to this document. CXLs for trinexapac are not available.

For the purpose of this MRL review, the critical uses of trinexapac currently authorized within the EU, have been collected by the RMS. Additional clarifications were also provided during the

[6] Commission Directive 2006/64/EC of 18 July 2006, OJ L 206, 27.7.2006, p. 107-111.
[7] Regulation (EU) No 540/2011 of 25 May 2011, OJ L 153, 11.6.2011, p. 1-186.
[8] Regulation (EC) No 1107/2009 of 21 October 2009, OJ 309, 24.11.2009, p. 1–50.

Members States Consultation (The Netherlands, 2011). All GAPs and comments are included in Appendix A. They include a single application in several cereal crops at growth stage BBCH 49 with application rates up to 180 g a.s./ha in northern Europe and up to 200 g a.s./ha in southern Europe. They also include a single application on poppy at BBCH 55 both in northern and southern Europe and on rape seed at BBCH 39 in northern Europe with application rate up to 380 g a.s./ha. The reported GAPs also refer to a single application in grass in northern Europe with application rate up to 200 g a.s./ha carried out at growth stage BBCH 39 at the latest. The RMS did not report any use authorised in third countries that might have a significant impact on international trade.

ASSESSMENT

EFSA bases its assessment on the PROFile submitted by the RMS, the Draft Assessment Report (DAR) and its addendum (The Netherlands, 2003, 2005), the conclusion on the peer review of the pesticide risk assessment of the active substance (EFSA, 2005) and the Dutch evaluation report submitted during the Member States consultation (The Netherlands, 2011). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation of the Authorization of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011[9] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2000, 2010a, 2010b, 2011).

It should be noted that the peer review of trinexapac under Directive 91/414/EEC mainly relied on the ethyl ester of trinexapac. The data reported below therefore relate to the acid variant of trinexapac, unless otherwise specified. These data are considered appropriate to support also the use of trinexapac and its salts because trinexapac-ethyl is readily hydrolysed to trinexapac acid in plants and livestock (see sections 3.1.1.1 and 3.2.2).

1. Methods of analysis

1.1. Methods for enforcement of residues in food of plant origin

During the peer review under Directive 91/414/EEC, an analytical method using HPLC-MS/MS and its ILV were evaluated and adequately validated for the determination of trinexapac (acid) and its salts in plant matrices with an LOQ of 0.02 g/kg in high water content (broad beans whole plant and dry broad beans seeds) commodities and with an LOQ of 0.01 mg/kg in high water content (apple) and high fat (oilseed rape) commodities (The Netherlands, 2005). Nevertheless, as apples are a borderline crop, findings are considered, in this case, to be applicable to acidic matrices as well.

Hence it is concluded that the sum of trinexapac (acid) and its salts expressed as trinexapac can be enforced in food of plant origin with a LOQ of 0.02 mg/kg in dry commodities and with an LOQ of 0.01 mg/kg in high fat content, high water content and acidic commodities.

1.2. Methods for enforcement of residues in food of animal origin

During the peer review under Directive 91/414/EEC, analytical method using HPLC-MS/MS and its ILV were evaluated and adequately validated for the determination of trinexapac (acid) and its salts in food of animal origin with a LOQ of 0.01 mg/kg in muscle, fat, eggs, kidney and liver, and with a LOQ of 5µg/L in milk (The Netherlands, 2005).

[9] Regulation (EU) No 546/2011 of 10 June 2011. OJ L 155, 11.06.2011, p. 127-175.

Hence it is concluded that the sum of trinexapac (acid) and its salts expressed as trinexapac can be enforced in food of animal origin with a LOQ of 0.01 mg/kg in muscle, fat, eggs, kidney and liver, and with a LOQ of 5µg/L in milk.

2. Mammalian toxicology

The toxicological assessment of trinexapac was peer reviewed under Directive 91/414/EEC and an ADI was established by EFSA (2005). The setting of an ARfD was not deemed necessary. The toxicological reference values are summarized in Table 2-1.

Table 2-1: Overview of the toxicological reference values

	Source	Year	Value (mg/kg bw/d)	Study relied upon	Safety factor
Trinexapac-ethyl					
ADI	EFSA	2005	0.32	One-year oral toxicity dog	100
ARfD	EFSA	2005	Allocation not necessary		

Toxicological reference values, which are based on studies carried out with trinexapac-ethyl, can also be considered relevant for trinexapac given the rather low conversion factor[10] of 1.11 for molecular weights and the fast hydrolysis of parent trinexapac-ethyl into trinexapac confirmed by the rat metabolism studies.

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

Metabolism of trinexapac-ethyl was investigated for foliar applications on cereals (wheat, rice) and on pulses and oilseed (rape) using [^{14}C-cyclohexyl]-trinexapac-ethyl. The basic characteristics of these metabolism studies are summarised in table 3-1.

The proposed metabolic pathway of trinexapac-ethyl in plants includes hydrolysis of the ester bond to trinexapac (EFSA, 2005). Further degradation proceeds via stepwise oxidation/decarboxylation after cleavage of the 6-membered ring yielding saturated and unsaturated tricarboxylated acids such as CGA 275537[11] and CGA 312753[12], which is an intermediate of the citric acid cycle (Krebs cycle). From the intermediates of the citric acid cycle and their breakdown products, sugars, fatty acids and certain amino acids are formed by de-novo synthesis. In wheat the ring cleavage occurs also on the

[10] Conversion factor for molecular weight: 1.11 calculated based on molar mass ratio of trinexapac-ethyl/trinexapac
[11] CGA275537 : 1,2,3-propanetricarboxylic acid (tricarballylic acid) (see Appendix E)
[12] CGA312753 : 12,3-propene tricarboxylic acid (trans aconitic acid) (see Appendix E)

parent molecule yielding the mono-ethylester of the aconitic acid. In rape trinexapac is reduced to CGA 351210[13], and subsequent conjugation with sugars occurs.

Table 3-1: Summary of available metabolism studies in plants

Group	Crop	Label position	Application and sampling details				
			Method, F or G [(a)]	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks
Pulses and oilseeds	Rape	[^{14}C-cyclohexyl]-trinexapac-ethyl	Foliar treatment, G	0.40	1	0.5 h, 14 and 65	
Cereals	Wheat	[^{14}C-cyclohexyl]-trinexapac-ethyl	Foliar treatment, G	0.15	1	0.5, 4 h, 1,2 7, 14 and 21	
Cereals	Wheat	[^{14}C-cyclohexyl]-trinexapac-ethyl	Foliar treatment, F	0.15	1	3 h, 25, 48 and 71	
Cereals	Rice	[^{14}C-cyclohexyl]-trinexapac-ethyl	Foliar treatment, G	Scenario 1: 0.040 Scenario 2: 0.16	1	Scenario 1: 1 h,7, 21, 60 and 82 Scenario 2: 60	

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G)

The major residue component found in all edible parts was trinexapac, formed by hydrolysis of the ester bond of trinexapac-ethyl (EFSA, 2005). Trinexapac represented up to 28% of the total residue in wheat grain, up to 30% in rape oil and meal, and up to 36% in rice grain. Other metabolites were present in relatively low levels, while a part of the residue was also associated with plant matrices. In plant products intended for animal feed, the major residue components were trinexapac (wheat straw), CGA 275537 (rice straw), and CGA 351210, free and conjugated (rape stalks, pods and seeds/meal). A part of the residue was also found to be associated with plant matrices (glucose, lipids, cellulose, pectin, and lignin). The metabolites CGA 351210 and CGA 275537 were neither found in the rat metabolism nor in livestock animals. Metabolite CGA 275537 has been tested and was not regarded to be of toxicological concern. However, no toxicity assessment has been provided for metabolite CGA 351210, which was found in rape matrices (seeds, oil, meal, pods, stalks), but not at significant level in oil. Since rape was not a representative use within the evaluation process for Annex I inclusion of trinexapac, this point was not further addressed during peer review.

No additional information was provided in the framework of this review. The metabolite CGA 351210 represented 16% of the TRR in rape seed oil and pods and 28% in stalks while trinexapac represented respectively 3.5%, 18.4% and 9.7% of the TRR in these crops. Moreover, absolute levels of CGA 351210 in oil were very low (approx. 0.005 mg/kg) and pods and stalks are neither used as food nor feed. Such levels of exposure are unlikely to represent a risk for consumers, especially when considering the high toxicological reference values of the parent compound and the similarity of chemical structure between parent and metabolite. Consequently, there is no need to include the metabolite in the residue definition.

[13] CGA351210 : 4-(cyclopropyl-alpha-hydroxy-methylene)-3,5-dioxocyclohexane methanol(see Appendix E)

Consequently, trinexapac is by far the predominating residue component in edible plant parts of cereals and oilseeds, whereas the applied trinexapac-ethyl is rapidly degraded to undetectable levels. Nevertheless, different salts of the acid form might be present. It is hence proposed to define the residue as trinexapac (acid) and its salts expressed as trinexapac for enforcement and risk assessment purposes instead of trinexapac only as proposed in the peer review. Validated analytical methods for enforcement of the proposed residue definition are available (see also section 1.1).

3.1.1.2. Magnitude of residues

According to the RMS, the active substance trinexapac is authorised for outdoor foliar treatment in barley, rye, wheat, dry beans and poppy seed in northern and southern Europe and on oats, rape seed and grass, in northern Europe (see Appendix A). To assess the magnitude of trinexapac residues resulting from these GAPs, EFSA considered all residues trials reported in the PROFile by the RMS. All available residues trials that, according to the RMS, comply with the authorised GAPs, are summarized in Table 3-2.

The number of residues trials and extrapolations were evaluated in view of the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (EC, 2011). A sufficient number of trials complying with the GAP was reported by the RMS for all crops under assessment, except in the following cases:

- For dry bean, the number of trials reported is not compliant with the data requirements for each area. As residues in northern Europe are higher than in southern Europe, MRL proposals cannot be based on a combined dataset for northern and southern Europe. Although tentative MRL and risk assessment values can be derived from the available data, 4 additional trials complying with each GAP (northern and the southern Europe) are still required. During the consultation of Member States, The Netherlands informed EFSA that the trials required are currently ongoing.
- For poppy seed, no trials are available and 4 trials complying with each GAP (northern and southern Europe) are still required. No MRL or risk assessment values can be derived for this crop.
- For the southern use on small grain cereals, only 6 residues trials on barley are available while 8 trials are normally required. However, a large number of residues trials supporting the northern outdoor GAP is available and residues in northern and southern Europe were found to be in the same range. Further trials supporting the southern GAP are therefore not required and MRL and risk assessment values are derived from the combined northern and southern datasets.
- For grass, no trials supporting the outdoor northern GAP are available and no MRL or risk assessment values can be derived. At least 4 residue trials compliant with the northern outdoor GAP are required. EFSA highlights that an extrapolation from cereal straw to grass seed production hay was proposed during the Member States consultation (The Netherlands, 2011). This extrapolation was not accepted since grass for seed production can not be considered biologically identical to cereals. Moreover, hay resulting from grass seed production is not accurately defined in legislation and there is no European guidance available for extrapolation or consumption of this commodity.

The potential degradation of trinexapac during storage of the residues trials samples was also assessed. In the framework of the peer review, storage stability of trinexapac was demonstrated for a period of 24 months at -18 °C in commodities with high oil (rape seed) content as well as dry commodities (EFSA, 2005; The Netherlands, 2003). According to the RMS, all residues trial samples reported in the PROFile were stored in compliance with the above reported storage conditions and degradation of residues during storage of the trial samples is not expected.

Table 3-2: Overview of the available residues trials data

Commodity	Residue region [a]	Outdoor /Indoor	Individual trial results (mg/kg)		Median residue (mg/kg) [b]	Highest residue (mg/kg) [c]	MRL proposal (mg/kg)	Median CF [d]	Comments
			Enforcement	Risk assessment					
Residue definition for enforcement and risk assessment: sum of trinexapac (acid) and its salts, expressed as trinexapac									
Beans (dry)	NEU	Outdoor	2.3; 4.11; 5.0; 5.38	2.3; 4.11; 5.0; 5.38	**4.56**	**5.38**	**10 (tentative)**	1.00	Trials compliant with GAP. Rber = 10.57 Rmax = 11.26
	SEU	Outdoor	1.86; 2.2; 2.3; 4.05	1.86; 2.2; 2.3; 4.05	2.25	4.05	8	1.00	Trials compliant with GAP. Rber = 7.22 Rmax = 7.66
Poppy seed	NEU	Outdoor	-	-	-	-	-	-	No residues trials available. Extrapolation from rape seed not possible (GAPs different).
	SEU	Outdoor	-	-	-	-	-	-	No residues trials available. Extrapolation from rape seed not possible (GAPs different).
Rape seed	NEU	Outdoor	0.04; 0.12; 0.13; 0.15; 0.15; 0.16; 0.19; 0.24; 0.24; 0.26; 0.27; 0.29; 0.29; 0.31; 0.33; 0.64; 0.64; 0.64; 0.90; 1.0	0.04; 0.12; 0.13; 0.15; 0.15; 0.16; 0.19; 0.24; 0.24; 0.26; 0.27; 0.29; 0.29; 0.31; 0.33; 0.64; 0.64; 0.64; 0.90; 1.0	0.27	1.00	2.00	1.00	Trials compliant with GAP. Rber = 1.13 Rmax = 0.99

Commodity	Residue region [a]	Outdoor /Indoor	Individual trial results (mg/kg)		Median residue (mg/kg) [b]	Highest residue (mg/kg) [c]	MRL proposal (mg/kg)	Median CF [d]	Comments
			Enforcement	Risk assessment					
Cereal grain (barley, oat, rye and wheat)	NEU & SEU	Outdoor	3x<0.02; 2x0.02; 0.05; 0.06; 3x0.07; 0.08; 2x 0.09; 0.10;2x 0.14; 2x0.18; 0.19; 0.20, 2x0.24; 0.44	3x<0.02; 2x0.02; 0.05; 0.06; 3x0.07; 0.08; 2x 0.09; 0.10;2x 0.14; 2x0.18; 0.19; 0.20, 2x0.24; 0.44	0.09	0.44	0.50	1.00	Trials compliant with GAP. Combined dataset of northern trials on barley (6), rye (4) and wheat (6) with 0.15-0.25 kg a.s./ha at BBCH 45-51 and southern trials on barley (6) with 0.15-0.25 kg a.s./ha at BBCH 31-32 supporting all small grain cereal GAPs (residues were similar). Rber = 0.36 Rmax = 0.35
Cereal straw (barley, oat, rye and wheat)	NEU & SEU	Outdoor	5x<0.02; 3x<0.04; 4x0.04; 2x0.05; 3x0.06; 0.07; 2x0.12; 0.13; 0.14	5x<0.02; 3x<0.04; 4x0.04; 2x0.05; 3x0.06; 0.07; 2x0.12; 0.13; 0.14	0.04	0.14	0.20	1.00	Trials compliant with GAP. Combined dataset of northern trials on barley (6), rye (4) and wheat (6) with 0.15-0.25 kg a.s./ha at BBCH 45-51 and southern trials on barley (6) with 0.15-0.25 kg a.s./ha at BBCH 31-32 supporting all small grain cereal GAPs (residues were similar). Rber = 0.13 Rmax = 0.14
Grass	-	-	-	-	-	-	-	-	No residue trials available.

(a): NEU (Northern and Central Europe), SEU (Southern Europe and Mediterranean), EU (i.e outdoor use) or Import (country code) (EC, 2011).
(b): Median value of the individual trial results according to the enforcement residue definition.
(c): Highest value of the individual trial results according to the enforcement residue definition.
(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residues trial.
(*): Indicates that the MRL is set at the limit of analytical quantification.

Consequently, for cereals and rape seed the available residues data are considered sufficient to derive adequate MRL proposals as well as risk assessment values. For dry beans, the available residues data are considered sufficient to derive tentative MRL only. For poppy seed, no residue data are available. Tentative MRLs were derived for cereals straw in view of the future need to set MRLs in feed items.

3.1.1.3. Effect of industrial processing and/or household preparation

The effect of processing on the nature of trinexapac-ethyl and trinexapac residues was investigated in the framework of the peer review. For trinexapac-ethyl, a study was conducted simulating representative hydrolytic conditions for pasteurisation (20 minutes at 90°C, pH 4), boiling/brewing/baking (60 minutes at 100°C pH 5) and sterilisation (20 minutes at 120°C, pH 6) (The Netherlands, 2003). This study showed that trinexapac-ethyl is hydrolytically stable under these conditions with negligible degradation (EFSA, 2005).

For trinexapac, a study was also conducted simulating pasteurization (25 minutes at 90°C, pH 4), boiling/brewing/baking (60 minutes at 100°C pH 5) and sterilisation (20 minutes at 120°C, pH 6) (The Netherlands, 2005). This study showed that at the end of incubation, trinexapac had degraded and represented 51-59% of the total radioactivity (EFSA, 2005). Degradation products identified were CGA 313458[14] (16-21%) and CGA 113745[15] (9.6-12%), which haven't been found in rat metabolism. CGA 313458 was tested and considered of no toxicological concern. According to the RMS, the toxicological assessment of CGA 113745 might be covered by the assessment of CGA 158377[16] since the ethyl ester bond of CGA 158377 is likely to be hydrolysed in the primary metabolic step, yielding CGA 113745. However, a complete toxicology package for CGA 158377 has also not been submitted. Based on the critical uses of trinexapac currently authorized within the EU, processing studies are not mandatory, since the TMDI represents less than the trigger value of 10% ADI. Therefore further data can currently not be considered essential. However, it is not possible to conclude that for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable.

Studies investigating the magnitude of residues in processed commodities of barley, wheat and rye were also reported in the framework of the peer review (EFSA, 2005). An overview of all available processing studies is available in Table 3-3, which were all carried out with incurred residues. The processing factors reported for barley, wheat and rye should be considered indicative because it was not possible to set a reliable residue definition in processed commodities and, in the case of wheat and rye, there are not enough processing studies available; a minimum of 3 processing studies is normally required.

In this case however, further processing studies are not required as they are not expected to affect the outcome of the risk assessment. If there would be the intention to derive more robust processing factors, in particular for enforcement purposes, additional processing studies would be required.

[14] CGA313458 : (2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid) or 3-carboxy-7-cyclopropyl-5,7-diketo-heptanoic acid (see appendix E)
[15] CGA 113745 : 3,5-dioxocyclohexanecarboxylic acid (see appendix E)
[16] CGA 158377 : 3,5-dioxocyclohexanecarboxylic acid ethylester (see appendix E)

Table 3-3: Overview of the available processing studies

Processed commodity	Number of studies	Median PF [(a)]	Median CF [(b)]	Comments
Indicative processing factors (limited dataset)				
Barley, brewing malt	8	0.70	1.00	-
Barley, beer	8	0.20	1.00	-
Rye, whole-meal flour	1	1.00	1.00	Processing studies performed with wheat may be extrapolated to rye as well.
Rye, whole-meal bread	1	0.60	1.00	Processing studies performed with wheat may be extrapolated to rye as well.
Rye, white flour	1	0.30	1.00	Processing studies performed with wheat may be extrapolated to rye as well.
Rye, bran	1	3.80	1.00	Processing studies performed with wheat may be extrapolated to rye as well.
Wheat, whole-meal flour	1	1.00	1.00	-
Wheat, whole-meal bread	1	0.60	1.00	-
Wheat, white flour	1	0.30	1.00	-
Wheat, bran	1	3.80	1.00	-

(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
(b): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

3.1.2. Rotational crops

All crops evaluated in the framework of this MRL review might be grown in rotation with other crops. During the peer review under Directive 91/414/EEC, it was demonstrated that DT_{90} values for trinexapac were below the trigger value of 100 days but DT_{90} values for trinexapac-ethyl were shown to exceed the trigger value (EFSA, 2005). For trinexapac, a detailed assessment of the nature and magnitude of trinexapac-ethyl residues is therefore considered relevant.

The EFSA conclusion (EFSA, 2005) and the DAR on trinexapac (The Netherlands, 2003) report a confined rotational crop study for trinexapac-ethyl, which was performed on representative crops for root and tuber vegetables, leafy vegetables and cereals. Data are summarized in table 3-4.

In all crops at all plant-back intervals, residue levels were at or below the LOQ (<0.001 mg/kg) and too low for identification. Hence, no metabolic pattern could be identified but no significant residue levels are to be expected in rotational crops following application of trinexapac-ethyl at a rate of 0.15 kg as/ha. Considering the study was carried out on a bare soil and that the maximum application rate of the critical uses of trinexapac currently authorized within the EU amounts to 0.38 kg as/ha, residues level in rotational commodities are not expected to exceed 0.01 mg/kg. No additional data on the magnitude of residues are necessary.

Table 3-4: Summary of available metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details				
			Method, F or G [(a)]	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks
Leafy vegetables	Lettuce	[^{14}C-cyclohexyl]-trinexapac-ethyl	Bare soil spraying, F	0.15	99, 119	129, 169	-
Root and tuber vegetables	Sugar beet	[^{14}C-cyclohexyl]-trinexapac-ethyl	Bare soil spraying, F	0.15	343, 407, 496	387, 515, 693	-
Cereals	Winter wheat	[^{14}C-cyclohexyl]-trinexapac-ethyl	Bare soil spraying, F	0.15	173, 299, 343, 407	227, 479, 567, 695	-
	Corn	[^{14}C-cyclohexyl]-trinexapac-ethyl	Bare soil spraying, F	0.15	369, 407, 496	400, 476, 654	-

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G)

3.2. Nature and magnitude of residues in livestock

3.2.1. Dietary burden of livestock

Trinexapac is authorised for use on several crops that might be fed to livestock. The median and maximum dietary burdens were therefore calculated for the different groups of livestock using to the agreed European methodology (European Commission, 1996). The input values for all relevant commodities have been selected according to the recommendations of JMPR (FAO, 2009) and are summarized in the Table 3-5. For rape seed meal, a default processing factor of 2 has been included in the calculation in order to consider potential concentration of residues in this commodity. For wheat bran and rye bran the indicative processing factors derived under section 3.1.1.3 have been included in the calculation. Due to the lack of residue trials, grass was not included in the calculation. However, considering the overwhelming contribution of dry beans, this is not expected to have a major impact on the livestock dietary burden.

Table 3-5: Input values for the dietary burden calculation

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition : sum of trinexapac (acid) and its salts, expressed as trinexapac				
Wheat grain	0.09	Median residue	0.09	Median residue
Barley grain	0.09	Median residue	0.09	Median residue
Rye grain	0.09	Median residue	0.09	Median residue
Oat grain	0.09	Median residue	0.09	Median residue
Wheat bran	0.34	Median residue x PF	0.34	Median residue x PF
Rye bran	0.34	Median residue x PF	0.34	Median residue x PF
Wheat straw	0.04	Median residue	0.14	Highest residue

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Barley straw	0.04	Median residue	0.14	Highest residue
Rye straw	0.04	Median residue	0.14	Highest residue
Oat straw	0.04	Median residue	0.14	Highest residue
Beans(dry)	4.56	Median residue	4.56	Median residue
Rape seed	0.27	Median residue	0.27	Median residue
Rape seed meal	0.53	Median residue x 2	0.53	Median residue x 2

The results of the calculations are reported in Table 3-6. The calculated dietary burdens for all groups of livestock were found to exceed the trigger value of 0.1 mg/kg DM. Further investigation of residues is therefore required in all commodities of animal origin.

Table 3-6: Results of the dietary burden calculation

	Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Dairy ruminants	0.0492	0.0484	Beans(dry)	1.3673	Yes
Meat ruminants	0.0568	0.0572	Beans(dry)	1.3212	Yes
Poultry	0.1082	0.1082	Beans(dry)	1.7177	Yes
Pigs	0.0927	0.0927	Beans(dry)	2.3187	Yes

3.2.2. Nature of residues

The nature of trinexapac-ethyl residues in commodities of animal origin was investigated in the framework of Directive 91/414/EEC (EFSA, 2003). Reported metabolism studies include three studies in dairy goats and one study in laying hens. These studies are summarized in the Table 3-7.

The metabolism in lactating goats and laying hens was investigated with trinexapac-ethyl while trinexapac is the major residue components in livestock feed. As such, the livestock metabolism studies with trinexapac-ethyl might be considered less relevant in first instance. But due to the fast and extensive metabolism of trinexapac-ethyl to trinexapac in animals, the results gained from studies with trinexapac-ethyl are considered applicable for the evaluation.

After oral dosing with highly exaggerated doses of trinexapac-ethyl, highest residue concentrations are found in kidneys of both species (0.50-42 mg eq/kg for lactating goat and 0.056-3.3 mg eq/kg for laying hens). Relatively low residue levels are observed in milk and eggs (0.008-0.83 mg eq/kg for milk, 0.005-0.095 mg eq/kg for egg yolk and 0.007-0.55 mg eq/kg for egg white). Residue concentrations reach plateau levels in milk after about 2 to 3 days and in eggs after about 2 days. Trinexapac is the major residue component identified in milk, meat and offal from ruminants, accounting for about 66-97% TRR. In one of the goat studies, metabolite CGA 113745 was also found in liver, kidney and fat (6-16% TRR), however, absolute levels are low (<0.4 mg/kg) considering the exaggerated dose administered to the animals (*ca* 300 N) and would be negligible at the estimated highest likely feeding rate in practice (N).

Table 3-7: Summary of available metabolism studies in livestock

Group	Species	Label position	No of animal	Application details		Sample details	
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time
Lactating ruminants	Goat	[1,2-^{14}C-cyclohexyl] trinexapac-ethyl	2	0.2 (low dose) 20 (high dose)	4	Milk	Daily
						Urine and feaces	Daily
						Tissues	After sacrifice
						Blood	0.5, 1, 3, 6, 12 and 76 hours after first dose
	Goat	[1,2-^{14}C-cyclohexyl] trinexapac-ethyl	2	0.2 (low dose) 20 (high dose)	4	Milk	p.m. on days 1, 2 and 3
						Urine	-
						Tissues	After sacrifice
	Goat	[1,2,6-^{14}C-cyclohexyl] trinexapac-ethyl	2	3	4	Milk	Twice daily
						Urine and feaces	Daily
						Tissues	After sacrifice
						Blood	Just before sacrifice
Laying poultry	Hens	[1,2-^{14}C-cyclohexyl] trinexapac-ethyl	6	0.4 (low dose) 20 (high dose)	4	Eggs	Daily
						Tissue	After sacrifice
						Blood	Just prior sacrifice

In poultry meat, offal, and egg yolk, again, trinexapac is the major residue component representing about 60% TRR, 10-80% TRR, and 28% TRR, respectively. The exception is egg white, in which trinexapac-ethyl is dominating (44% TRR), although being present at very low levels (0.0017 mg eq/kg).

The metabolic pathway of the trinexapac-ethyl in livestock comprises of hydrolysis of the ester bond to the formation of trinexapac. CGA 113745 was the only other metabolite identified in goat milk and tissues. The observed metabolic pathway of trinexapac-ethyl in livestock is comparable to the rat, in which trinexapac is the major and only residue component of significance. Therefore it is proposed to define the residue in animal products as the sum of trinexapac (acid) and its salts, expressed as trinexapac, both for enforcement and risk assessment purposes. Validated analytical methods for enforcement of the proposed residue definition are available (see also section 1.2).

In the framework of the peer review, the proposed residue definition was not considered to be fat soluble based on the fact that the log $P_{o/w}$ of trinexapac is lower than 3 (EFSA, 2005).

3.2.3. Magnitude of residues

During the peer review of Directive 91/414/EEC the magnitude of trinexapac residues in livestock was investigated in the feeding study with lactating cows (The Netherlands, 2003). Three groups of lactating cows, each consisting of three animals, were dosed for 28-29 days with trinexapac at levels of 0.068, 0.21 and 0.71 mg trinexapac/kg bw/day. Detailed results are reported in Table 3-8.

According to the above mentioned metabolism study in lactating cows, kidney was the only tissue of all samples analysed were a clear dose dependent increase of trinexapac residues was found (The Netherlands, 2003). The residues in muscle and fat were below or around the LOQ of 0.02 mg/kg. In the liver the residue level was only detected in the highest dose group just above the LOQ. Residues in milk samples were only found in the highest dosed group, reaching 0.011 mg/kg. No detectable residues are expected in ruminant products at a nominal intake of trinexapac via feed (0.14-0.23 mg/kg feed).

For poultry, no livestock feeding is available but no measurable residues are expected based the calculated dietary burtden for poultry and the available poultry metabolism study.

The demonstrated storage stability of trinexapac in animal products was evaluated under the peer review of Directive 91/414/EEC (The Netherlands, 2003). Studies demonstrated storage stability of trinexapac in milk and animal tissues for up to 3 months when stored deep frozen but the storage conditions of samples of the livestock feeding study were not reported. In order to exclude degradation of residues during storage of the livestock feeding samples, a confirmation that livestock feeding samples were stored in compliance with these conditions is still desirable.

Based on the available livestock feeding study and the poultry metabolism study, it is concluded that significant residues in edible matrices of ruminants, poultry and pigs are not expected and that MRLs for these commodities can be established at the enforcement LOQ, except for ruminant kidney. MRLs calculated for kidney by EFSA in the framework of this review are significantly higher than the MRLs calculated by the RMS in the framework of the peer review (The Netherlands, 2003) because dietary burden of livestock is now mainly driven by dry beans, which were not yet supported in the framework of the peer review.

Table 3-8: Overview of the values derived from the livestock feeding studies

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[b]	Highest residue (mg/kg)[c]	MRL proposal (mg/kg)[d]	CF for RA
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)	No	Result for enf.		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
Enforcement residue definition : sum of trinexapac (acid) and its salts, expressed as trinexapac												
Pig meat	0.0927	0.0927	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				
			0.71	1	0.02	0.02	0.02	0.02				
Pig fat	0.0927	0.0927	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				
			0.71	1	0.02	0.02	0.02	0.02				
Pig liver	0.0927	0.0927	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				
			0.71	1	0.03	0.03	0.03	0.03				
Pig kidney	0.0927	0.0927	0.07	1	0.03	0.03	0.03	0.03	0.03	0.03	0.05	1.00
			0.21	1	0.05	0.05	0.05	0.05				
			0.71	1	0.29	0.29	0.29	0.29				
Ruminant meat	0.0572	0.0568	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				
			0.71	1	0.02	0.02	0.02	0.02				
Ruminant fat	0.0572	0.0568	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[b]	Highest residue (mg/kg)[c]	MRL proposal (mg/kg)[d]	CF for RA
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)	No	Result for enf.		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
			0.71	1	0.02	0.02	0.02	0.02				
Ruminant liver	0.0572	0.0568	0.07	1	0.02	0.02	0.02	0.02	0.01	0.01	0.01*	1.00
			0.21	1	0.02	0.02	0.02	0.02				
			0.71	1	0.03	0.03	0.03	0.03				
Ruminant kidney	0.0572	0.0568	0.07	1	0.03	0.03	0.03	0.03	0.03	0.03	0.05	1.00
			0.21	1	0.05	0.05	0.05	0.05				
			0.71	1	0.29	0.29	0.29	0.29				
Milk	0.0484	0.0492	0.07	1	0.01	n.a	0.01	n.a	0.01	0.01	0.005*	1.00
			0.21	1	0.01	n.a	0.01	n.a				
			0.71	1	0.01	n.a	0.01	n.a				

n.a.: not applicable – only the mean values are considered for calculating MRLs in milk

(*): Indicates that the MRL is set at the limit of analytical quantification.

(a): The feeding study was carried out with ruminants but for calculation of MRLs and risk assessment values results were interpolated with the dietary burden of pigs; according to the metabolism pathway, an extrapolation between ruminant and pig is acceptable

(b): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009).

(c): Highest residue value (tissues, eggs) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009).

(d): The median conversion factor for enforcement to risk assessment.

4. Consumer risk assessment

Chronic exposure calculations for all crops supported in the framework of this review were performed using revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo) (EFSA, 2007). Input values for the intake calculations were derived in compliance with Appendix D and are summarized in Table 4-1. The median residue and highest residue values selected for chronic calculation are based on the residue levels in the raw agricultural commodities. For poppy seed no residues trial was provided, EFSA therefore decided to include the existing EU MRL for indicative risk assessment. The contributions of other commodities, for which no authorised uses were reported in the framework of this review, were not included in the calculation.

Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.

Table 4-1: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition : sum of trinexapac (acid) and its salts, expressed as trinexapac				
Beans (dry)	4.56	Median residue (tentative)[(b)]	5.38	Highest residue[(b)]
Poppy seed	0.05	EU MRL[(c)]	0.05	EU MRL[(c)]
Rape seed	0.27	Median residue[(a)]	1.00	Highest residue[(a)]
Barley grain	0.09	Median residue[(a)]	0.44	Highest residue[(a)]
Oats grain	0.09	Median residue[(a)]	0.44	Highest residue[(a)]
Rye grain	0.09	Median residue[(a)]	0.44	Highest residue[(a)]
Wheat grain	0.09	Median residue[(a)]	0.44	Highest residue[(a)]
Swine meat	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]
Swine fat (free of lean meat)	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]
Swine liver	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]
Swine kidney	0.03	Median residue[(a)]	0.03	Highest residue[(a)]
Ruminant meat	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]
Ruminant fat	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]
Ruminant liver	0.01	Median residue (=LOQ) [(a)]	0.01	Highest residue (=LOQ)[(a)]
Ruminant kidney	0.03	Median residue[(a)]	0.03	Highest residue[(a)]
Poultry meat	0.01	Median residue (=LOQ)[(a)]	0.01	Highest residue (=LOQ)[(a)]

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Poultry fat	0.01	Median residue (=LOQ)[a]	0.01	Highest residue (=LOQ)[a]
Poultry liver	0.01	Median residue (=LOQ)[a]	0.01	Highest residue (=LOQ)[a]
Ruminant milk	0.005	Median residue (=LOQ)[a]	0.005	Highest residue (=LOQ)[a]
Birds' eggs	0.01	Median residue (=LOQ)[a]	0.01	Highest residue (=LOQ)[a]

(a): At least one relevant GAP reported by the RMS is fully supported by data for this commodity; the risk assessment values derived in section 3 are used for the exposure calculations.
(b): Use reported by the RMS is not fully supported by data but the risk assessment values derived in section 3 are used for indicative exposure calculations.
(c): Use reported by the RMS is not supported by data; the existing EU MRL is used for indicative exposure calculations.

The calculated exposures were compared with the toxicological reference value derived for trinexapac (see Table 2-1); detailed results of the calculations are presented as EU scenario 1 in Appendix B.1. The highest chronic exposure was calculated for UK toddlers, representing 1.2% of the ADI.

Based on the above calculations, EFSA concludes that the use of trinexapac on crops fully supported by data (footnote a in Table 4-1), is acceptable with regard to consumer exposure. For dry beans and poppy seeds, major uncertainties remain due to the data gaps identified in section 3, but considering a tentative MRL or the current EU MRL in the exposure calculation did not indicate a risk to consumers.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The toxicological profile of trinexapac was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI of 0.32 mg/kg bw/d. ADI was derived from studies carried out with trinexapac-ethyl but it may be applied to trinexapac. An ARfD was not deemed necessary for this active substance.

Primary crop metabolism of trinexapac was investigated following a single foliar application in wheat, rice and rape seed, hereby covering two different crop groups. Metabolic patterns in the different studies were shown to be similar and the relevant residue for enforcement and risk assessment in all plant commodities could be defined as the sum of trinexapac (acid) and its salts, expressed as trinexapac. A validated analytical method for enforcement of the proposed residue definitions is available, with an LOQ of 0.02 mg/kg in commodities with high water content and in dry commodities, and with an LOQ of 0.01 mg/kg in commodities with a high fat content.

Regarding the magnitude of residues in all crops reported by the RMS, a sufficient number of supervised residues trials is available for barley, oats, rye, wheat and rape seed, which allowed EFSA to estimate the expected residue concentrations in the relevant plant commodities and to derive appropriate MRLs. For dry beans, EFSA was only able to derive a tentative MRL while for poppy seeds no residues trials were available and no MRL could be derived.

In processed commodities, trinexapac-ethyl were shown to be stable during pasteurisation, boiling, brewing, baking and sterilisation. A study conducted with trinexapac however showed that at the end

of incubation, trinexapac had degraded and represented 51-59% of the total radioactivity and that two main metabolites are formed. One of them was not of toxicological concern but for the other metabolite the complete toxicology package has not been submitted. Nevertheless, based on the critical uses of trinexapac currently authorized within the EU, the overall chronic exposure represents less than 10% of the ADI and processing studies are not mandatory. Therefore further data are currently not considered essential. Studies investigating the magnitude of residues in processed commodities of barley and wheat and rye were also reported in the framework of the peer review but no robust processing factors for enforcement and risk assessment purposes could be derived from these studies. Further processing studies are currently not required as they are not expected to affect the outcome of the risk assessment. However, if there would be the intention from risk managers to derive more processing factors for enforcement purposes, additional processing studies might be required.

Occurrence of trinexapac residues in rotational crops was already investigated during the peer review of trinexapac. Confined rotational crop studies investigating the uptake of residues in lettuce, wheat, sugar beets and corn were reported. It was concluded that significant residues in rotational crops are not expected. These conclusions also apply to the GAPs of trinexapac supported in the framework of this review.

Based on the uses reported by the RMS, significant intakes were calculated for dairy ruminant, meat ruminants, poultry and pigs. Metabolism in poultry and lactating ruminants was sufficiently investigated and findings can be extrapolated to pigs as well. The relevant residue definition for both enforcement and risk assessment in poultry, ruminants and pigs was therefore defined as the sum of trinexapac (acid) and its salts, expressed as trinexapac. Based on the available livestock feeding study, it is also concluded that significant residues in edible matrices of ruminants, poultry and pigs are not expected and that MRLs for these commodities can be established at the LOQ, except for kidney where an MRL of 0.05 mg/kg is derived. A validated analytical method for enforcement of the proposed MRLs is available, with a LOQ of 0.01 mg/kg in animal tissues. For milk, the LOQ is proposed at 0.005 mg/kg.

Chronic consumer exposure resulting from the uses supported in the framework of this review was calculated and compared with the toxicological reference value derived for trinexapac. The highest chronic exposure was calculated for UK toddlers, representing 1.2% of the ADI. Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.

RECOMMENDATIONS

Based on the above assessment, EFSA does not recommend inclusion of this active substance in Annex IV to Regulation (EC) No 396/2005. MRL recommendations were derived in compliance with the decision tree reported in Appendix D (see table below for a summary). All MRL values listed as 'Recommended' in the table are sufficiently supported by data and therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL values listed in the table are not recommended for inclusion in Annex II because they require further consideration by risk managers (see table footnotes for details). In particular, certain tentative MRLs and existing EU MRLs still need to be confirmed by the following data:

- 4 additional residue trials supporting outdoor GAP on dry bean in southern and 4 additional residue trials in northern Europe;
- 4 residue trials supporting outdoor GAP on poppy seed in southern and 4 residue trials in northern Europe.

Moreover, in view of the future need to set MRLs in feed items, the following data might also be required:

- 4 residue trials supporting the northern GAP on grass;

If the above reported data gaps are not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level.

A minor deficiency was also identified in the assessment but this deficiency is not expected to impact either on the validity of the 'Recommended' MRLs or on the national authorisations. A confirmation that livestock feeding samples were stored in compliance with demonstrated storage conditions is therefore considered desirable but not essential.

Code number	Commodity	Existing EU MRL (mg/kg)	Outcome of the review	
			MRL (mg/kg)	Comment
Enforcement residue definition : sum of trinexapac (acid) and its salts, expressed as trinexapac				
300010	Beans (dry)	10	10	Further consideration needed[(a)]
401030	Poppy seed	0.05*	0.05	Further consideration needed[(b)]
401060	Rape seed	2	2	Recommended[(c)]
500010	Barley grain	0.5	0.5	
500050	Oats grain	0.5	0.5	
500070	Rye grain	0.5	0.5	
500090	Wheat grain	0.5	0.5	
1011010	Swine meat	0.05*	0.01*	
1011020	Swine fat (free of lean meat)	0.05*	0.01*	
1011030	Swine liver	0.05*	0.01*	
1011040	Swine kidney	0.05*	0.05	
1012010	Bovine meat	0.05*	0.01*	
1012020	Bovine fat	0.05*	0.01*	
1012030	Bovine liver	0.05*	0.01*	
1012040	Bovine kidney	0.05*	0.05	
1013010	Sheep meat	0.05*	0.01*	
1013020	Sheep fat	0.05*	0.01*	
1013030	Sheep liver	0.05*	0.01*	
1013040	Sheep kidney	0.05*	0.05	
1014010	Goat meat	0.05*	0.01*	
1014020	Goat fat	0.05*	0.01*	
1014030	Goat liver	0.05*	0.01*	
1014040	Goat kidney	0.05*	0.05	
1016010	Poultry meat	0.05*	0.01*	
1016020	Poultry fat	0.05*	0.01*	

Code number	Commodity	Existing EU MRL (mg/kg)	Outcome of the review	
			MRL (mg/kg)	Comment
1016030	Poultry liver	0.05*	0.01*	
1020010	Cattle milk	0.05*	0.005*	
1020020	Sheep milk	0.05*	0.005*	
1020030	Goat milk	0.05*	0.005*	
1030000	Birds' eggs	0.05*	0.01*	
-	Other products of plant and animal origin	See App. C	-	Further consideration needed (d)

(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.
(a): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers could be identified; no CXL is available (combination E-I in Appendix D).
(b): GAP evaluated at EU level is not supported by data but no risk to consumers could be identified for the existing EU MRL; no CXL is available (combination C-I in Appendix D).
(c): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination G-I in Appendix D).
(d): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either the specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix D).

DOCUMENTATION PROVIDED TO EFSA

1. Pesticide Residues Overview File (PROFile) on trinexapac prepared by the rapporteur Member State The Netherlands in the framework of Article 12 of Regulation (EC) No 396/2005. Submitted to EFSA on 24 February 2009. Last updated on 04 November 2009.

REFERENCES

EC (European Commission), 1996. Appendix G. Livestock Feeding Studies. 7031/VI/95 rev.4. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997b. Appendix B. General recommendations for the design, preparation and realization of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev.3. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414. SANCO/3029/99-rev.4. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2005. Review report for the active substance trinexapac. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 04 April 2006 in view of the inclusion of trinexapac in Annex I of Council Directive 91/414/EEC. SANCO/10011/2006-Final, 04 April 2006. Available online: http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection

EC (European Commission), 2006. Commission Directive 2006/64/EC of 18 July 2006, OJ L 206, 27.7.2006, p. 107-111.

EC (European Commission), 2008. Commission Regulation EC 149/2008/ of 29 January 2008, OJ L 258, 29.6.2006, p. 1-398.

EC (European Commission), 2010a. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010 Rev. 0, finalized in the Standing Committee on the Food Chain and Animal Health at its meeting of 23-24 March 2010. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2010b. Residue analytical methods. For post-registration control. SANCO/825/00-rev.8-1. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EC (European Commission), 2011. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.9. Available online: http://ec.europa.eu/food/plant/protection/resources/publications_en.htm

EFSA (European Food Safety Authority), 2005. Conclusion on the peer review of the pesticide risk assessment of the active substance trinexapac. *EFSA Scientific Report* (2005) 57, 1-70.

EFSA (European Food Safety Authority), 2007. Reasoned opinion on the potential chronic and acute risk to consumers' health arising from proposed temporary EU MRLs according to Regulation (EC) No 396/2005 on Maximum Residue Levels of Pesticides in Food and Feed of Plant and Animal Origin. 15 March 2007.

FAO (Food and Agriculture Organization of the United Nations), 2009. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed**.** Pesticide Residues. 2nd Ed. FAO Plant Production and Protection Paper 197, 264 pp.

The Netherlands, 2003. Draft assessment report on the active substance trinexapac prepared by the rapporteur Member State The Netherlands in the framework of Council Directive 91/414/EEC, October 2003.

The Netherlands, 2005. Addendum to the draft assessment report on the active substance trinexapacprepared by the rapporteur Member State The Netherlands in the framework of Council Directive 91/414/EEC, January 2005.

The Netherlands, 2011. Evaluation Report prepared under Article 12 of Regulation (EC) No 396/2005. Authorised uses to be considered for the review of the existing MRLs for trinexapac, October 2011.

APPENDIX A – GOOD AGRICULTURAL PRACTICES (GAPS)

Critical Outdoor GAPs for Northern Europe																				
Crop		Region	Outdoor/ Indoor	Member state or Country	Pests controlled	Formulation			Application							Application rate			PHI or waiting period (days)	Comments (max. 250 charachters)
Common name	Scientific name					Type	Content		Method	Growth stage		Number		Interval (days)		Min. rate	Max. rate	Rate Unit		
							Conc.	Unit		From BBCH	Until BBCH	Min.	Max.	Min.	Max.					
Beans (dry)	*Phaseolus vulgaris*	NEU	Outdoor	FR	Growth regulator				Foliar treatment - spraying	65	75	1	1			0,13	0,13	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 56d.
Poppy seed	*Papaver somniferum*	NEU	Outdoor	FR	Resistance to lodging				Foliar treatment - spraying		39	1	1			0,38	0,38	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 45d.
Rape seed	*Brassica napus*	NEU	Outdoor	NL	Resistance to lodging	EC	250,0	g/L	Foliar treatment - spraying	51	55	1	1			0,38	0,38	kg a.i./ha	n.a.	PHI determined by growth stage at application.
Barley	*Hordeum spp.*	NEU	Outdoor	FR	Growth regulator	EC	250,0	g/L	Foliar treatment - spraying	31	49	1	1			0,18	0,18	kg a.i./ha	n.a.	PHI determined by growth stage at application NL: BBCH 31-32, 200 g as/ha
Oats	*Avena fatua*	NEU	Outdoor	DE	Growth regulator	EC	222,0	g/L	Foliar treatment - spraying	31	37	1	1			0,13	0,13	kg a.i./ha	n.a.	PHI determined by growth stage at application.
Rye	*Secale cereale*	NEU	Outdoor	DE	Growth regulator	EC	222,0	g/L	Foliar treatment - spraying	31	39	1	1			0,13	0,13	kg a.i./ha	n.a.	PHI determined by growth stage at application. For triticale, the same GAP applies as for rye.
Wheat	*Triticum aestivum*	NEU	Outdoor	FR	Resistance to lodging	EC	250,0	g/L	Foliar treatment - spraying	25	49	1	1			0,13	0,13	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 51d.
Grass	*not specified*	NEU	Outdoor	UK, NL	Resistance to lodging	EC	250,0	g/L	Foliar treatment - spraying	30	39	1	1			0,20	0,20	kg a.i./ha	n.a.	Grass for seed production. PHI determined by growth stage at application.

Critical Outdoor GAPs for Southern Europe																				
Crop		Region	Outdoor/ Indoor	Member state or Country	Pests controlled	Formulation			Application							Application rate			PHI or waiting period (days)	Comments (max. 250 charachters)
Common name	Scientific name					Type	Content		Method	Growth stage		Number		Interval (days)		Min. rate	Max. rate	Rate Unit		
							Conc.	Unit		From BBCH	Until BBCH	Min.	Max.	Min.	Max.					
Beans (dry)	*Phaseolus vulgaris*	SEU	Outdoor	FR	Growth regulator	EC	250.0	g/L	Foliar treatment - spraying	65	75	1	1			0.13	0.13	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 56d.
Poppy seed	*Papaver somniferum*	SEU	Outdoor	FR	Resistance to lodging	EC	250.0	g/L	Foliar treatment - spraying		39	1	1			0.38	0.38	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 45d.
Barley	*Hordeum spp.*	SEU	Outdoor	FR	Growth regulator	EC	250.0	g/L	Foliar treatment - spraying	25	49	1	1			0.20	0.20	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 51d.
Rye	*Secale cereale*	SEU	Outdoor	FR	Growth regulator	EC	250.0	g/L	Foliar treatment - spraying	31	33	1	1			0.13	0.13	kg a.i./ha	n.a.	PHI determined by growth stage at application
Wheat	*Triticum aestivum*	SEU	Outdoor	FR	Growth regulator	EC	250.0	g/L	Foliar treatment - spraying	25	49	1	1			0.13	0.13	kg a.i./ha	n.a.	PHI determined by growth stage at application. FR: indicative PHI of 51d. For triticale, the same GAP applies as for rye.

APPENDIX B – PESTICIDE RESIDUES INTAKE MODEL (PRIMO)

Trinexapac			
Status of the active substance:	**Included**	Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.32**	ARfD (mg/kg bw):	**n.n.**
Source of ADI:	**EFSA**	Source of ARfD:	**EFSA**
Year of evaluation:	**2005**	Year of evaluation:	**2005**

Chronic risk assessment - refined calculations

	TMDI (range) in % of ADI minimum - maximum
	1
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
1.2	UK Toddler	1.1	Beans	0.1	Wheat	0.0	Birds' eggs	
0.8	UK Infant	0.7	Beans	0.1	Wheat	0.0	Oats	
0.6	UK vegetarian	0.5	Beans	0.1	Wheat	0.0	Oats	
0.4	WHO Cluster diet B	0.2	Wheat	0.1	Beans	0.0	Barley	
0.4	WHO cluster diet D	0.2	Wheat	0.1	Beans	0.0	Rye	
0.4	UK Adult	0.3	Beans	0.0	Wheat	0.0	Birds' eggs	
0.4	PT General population	0.2	Beans	0.1	Wheat	0.0	Rye	
0.3	ES child	0.2	Beans	0.1	Wheat	0.0	Milk and milk products: Cattle	
0.3	WHO Cluster diet F	0.1	Beans	0.1	Wheat	0.0	Rape seed	
0.3	IT kids/toddler	0.2	Wheat	0.1	Beans	0.0	Barley	
0.3	IE adult	0.2	Beans	0.1	Wheat	0.0	Barley	
0.3	DK child	0.2	Wheat	0.1	Rye	0.0	Oats	
0.3	NL child	0.1	Wheat	0.1	Beans	0.0	Milk and milk products: Cattle	
0.3	WHO cluster diet E	0.1	Wheat	0.0	Rape seed	0.0	Beans	
0.2	WHO regional European diet	0.1	Beans	0.1	Wheat	0.0	Rape seed	
0.2	IT adult	0.1	Wheat	0.1	Beans	0.0	Barley	
0.2	DE child	0.1	Wheat	0.0	Rye	0.0	Rye	
0.2	ES adult	0.1	Beans	0.1	Wheat	0.0	Barley	
0.1	NL general	0.1	Wheat	0.1	Beans	0.0	Barley	
0.1	SE general population 90th percentile	0.1	Wheat	0.0	Milk and milk products: Cattle	0.0	Rye	
0.1	FI adult	0.1	Beans	0.0	Wheat	0.0	Rye	
0.1	FR all population	0.1	Wheat	0.0	Milk and milk products: Cattle	0.0	Poultry: Meat	
0.1	DK adult	0.1	Wheat	0.0	Rye	0.0	Beans	
0.1	FR toddler	0.1	Wheat	0.0	Bovine: Meat	0.0	Birds' eggs	
0.1	LT adult	0.0	Rye	0.0	Wheat	0.0	Milk and milk products: Cattle	
0.1	FR infant	0.0	Milk and milk products: Cattle	0.0	Wheat	0.0	Bovine: Meat	
0.0	PL general population	0.0	Beans	0.0	Poppy seed		FRUIT (FRESH OR FROZEN)	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Trinexapac is unlikely to present a public health concern.

APPENDIX C – EXISTING EU MAXIMUM RESIDUE LIMITS (MRLS)

(Pesticides - Web Version - EU MRLs (File created on 16/03/2011 03:12 pm)

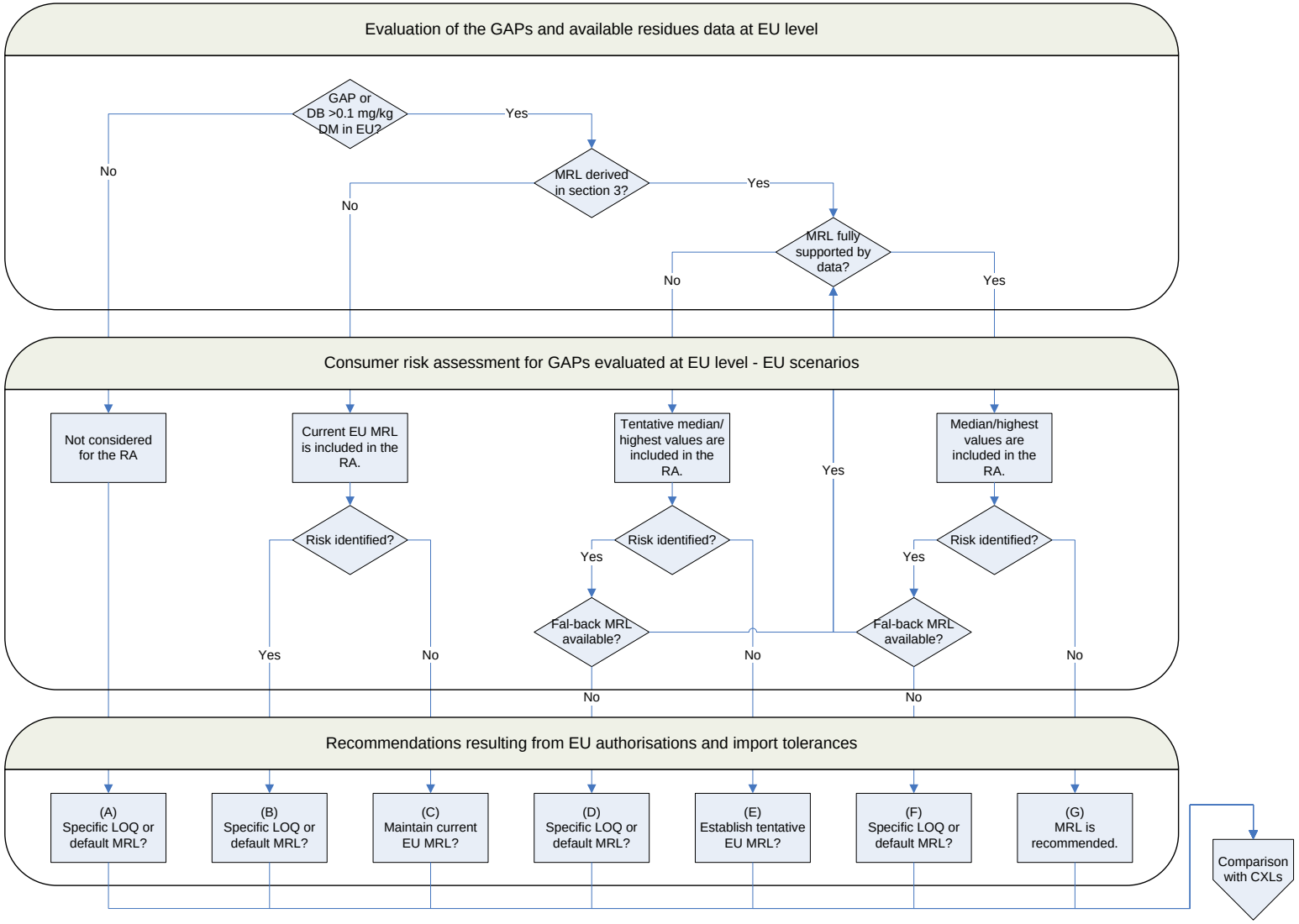
Code number	Groups and examples of individual products to which the MRLs apply (a)	Trinexapac
100000	1. FRUIT FRESH OR FROZEN; NUTS	0,05*
110000	(i) Citrus fruit	0,05*
110010	Grapefruit (Shaddocks, pomelos, sweeties, tangelo, ugli and other hybrids)	0,05*
110020	Oranges (Bergamot, bitter orange, chinotto and other hybrids)	0,05*
110030	Lemons (Citron, lemon)	0,05*
110040	Limes	0,05*
110050	Mandarins (Clementine, tangerine and other hybrids)	0,05*
110990	Others	0,05*
120000	(ii) Tree nuts (shelled or unshelled)	0,05*
120010	Almonds	0,05*
120020	Brazil nuts	0,05*
120030	Cashew nuts	0,05*
120040	Chestnuts	0,05*
120050	Coconuts	0,05*
120060	Hazelnuts (Filbert)	0,05*
120070	Macadamia	0,05*
120080	Pecans	0,05*
120090	Pine nuts	0,05*
120100	Pistachios	0,05*
120110	Walnuts	0,05*
120990	Others	0,05*
130000	(iii) Pome fruit	0,05*
130010	Apples (Crab apple)	0,05*
130020	Pears (Oriental pear)	0,05*
130030	Quinces	0,05*
130040	Medlar	0,05*
130050	Loquat	0,05*
130990	Others	0,05*
140000	(iv) Stone fruit	0,05*
140010	Apricots	0,05*
140020	Cherries (sweet cherries, sour cherries)	0,05*
140030	Peaches (Nectarines and similar hybrids)	0,05*
140040	Plums (Damson, greengage, mirabelle)	0,05*
140990	Others	0,05*
150000	(v) Berries & small fruit	0,05*
151000	(a) Table and wine grapes	0,05*
151010	Table grapes	0,05*
151020	Wine grapes	0,05*
152000	(b) Strawberries	0,05*
153000	(c) Cane fruit	0,05*
153010	Blackberries	0,05*
153020	Dewberries (Loganberries, Boysenberries, and cloudberries)	0,05*
153030	Raspberries (Wineberries)	0,05*
153990	Others	0,05*
154000	(d) Other small fruit & berries	0,05*
154010	Blueberries (Bilberries cowberries (red bilberries))	0,05*
154020	Cranberries	0,05*
154030	Currants (red, black and white)	0,05*
154040	Gooseberries (Including hybrids with other ribes species)	0,05*
154050	Rose hips	0,05*
154060	Mulberries (arbutus berry)	0,05*
154070	Azarole (mediteranean medlar)	0,05*
154080	Elderberries (Black chokeberry (appleberry), mountain ash, azarole, buckthorn (sea sallowthorn), hawthorn, service berries, and other treeberries)	0,05*
154990	Others	0,05*
160000	(vi) Miscellaneous fruit	0,05*
161000	(a) Edible peel	0,05*
161010	Dates	0,05*
161020	Figs	0,05*
161030	Table olives	0,05*
161040	Kumquats (Marumi kumquats, nagami kumquats)	0,05*
161050	Carambola (Bilimbi)	0,05*
161060	Persimmon	0,05*
161070	Jambolan (java plum) (Java apple (water apple), pomerac, rose apple, Brazilean cherry (grumichama), Surinam cherry)	0,05*
161990	Others	0,05*
162000	(b) Inedible peel, small	0,05*
162010	Kiwi	0,05*
162020	Lychee (Litchi) (Pulasan, rambutan (hairy litchi))	0,05*
162030	Passion fruit	0,05*
162040	Prickly pear (cactus fruit)	0,05*
162050	Star apple	0,05*
162060	American persimmon (Virginia kaki) (Black sapote, white sapote, green sapote, canistel (yellow sapote), and mammey sapote)	0,05*
162990	Others	0,05*
163000	(c) Inedible peel, large	0,05*
163010	Avocados	0,05*
163020	Bananas (Dwarf banana, plantain, apple banana)	0,05*
163030	Mangoes	0,05*
163040	Papaya	0,05*
163050	Pomegranate	0,05*
163060	Cherimoya (Custard apple, sugar apple (sweetsop) , llama and other medium sized Annonaceae)	0,05*
163070	Guava	0,05*
163080	Pineapples	0,05*
163090	Bread fruit (Jackfruit)	0,05*
163100	Durian	0,05*
163110	Soursop (guanabana)	0,05*
163990	Others	0,05*
200000	2. VEGETABLES FRESH OR FROZEN	
210000	(i) Root and tuber vegetables	
211000	(a) Potatoes	0,05*
212000	(b) Tropical root and tuber vegetables	1
212010	Cassava (Dasheen, eddoe (Japanese taro), tannia)	1
212020	Sweet potatoes	1
212030	Yams (Potato bean (yam bean), Mexican yam bean)	1
212040	Arrowroot	1
212990	Others	1
213000	(c) Other root and tuber vegetables except sugar beet	1
213010	Beetroot	1
213020	Carrots	1
213030	Celeriac	1
213040	Horseradish	1
213050	Jerusalem artichokes	1
213060	Parsnips	1
213070	Parsley root	1
213080	Radishes (Black radish, Japanese radish, small radish and similar varieties)	1
213090	Salsify (Scorzonera, Spanish salsify (Spanish oysterplant))	1
213100	Swedes	1
213110	Turnips	1
213990	Others	1
220000	(ii) Bulb vegetables	1
220010	Garlic	1
220020	Onions (Silverskin onions)	1
220030	Shallots	1
220040	Spring onions (Welsh onion and similar varieties)	1
220990	Others	1
230000	(iii) Fruiting vegetables	1
231000	(a) Solanacea	1

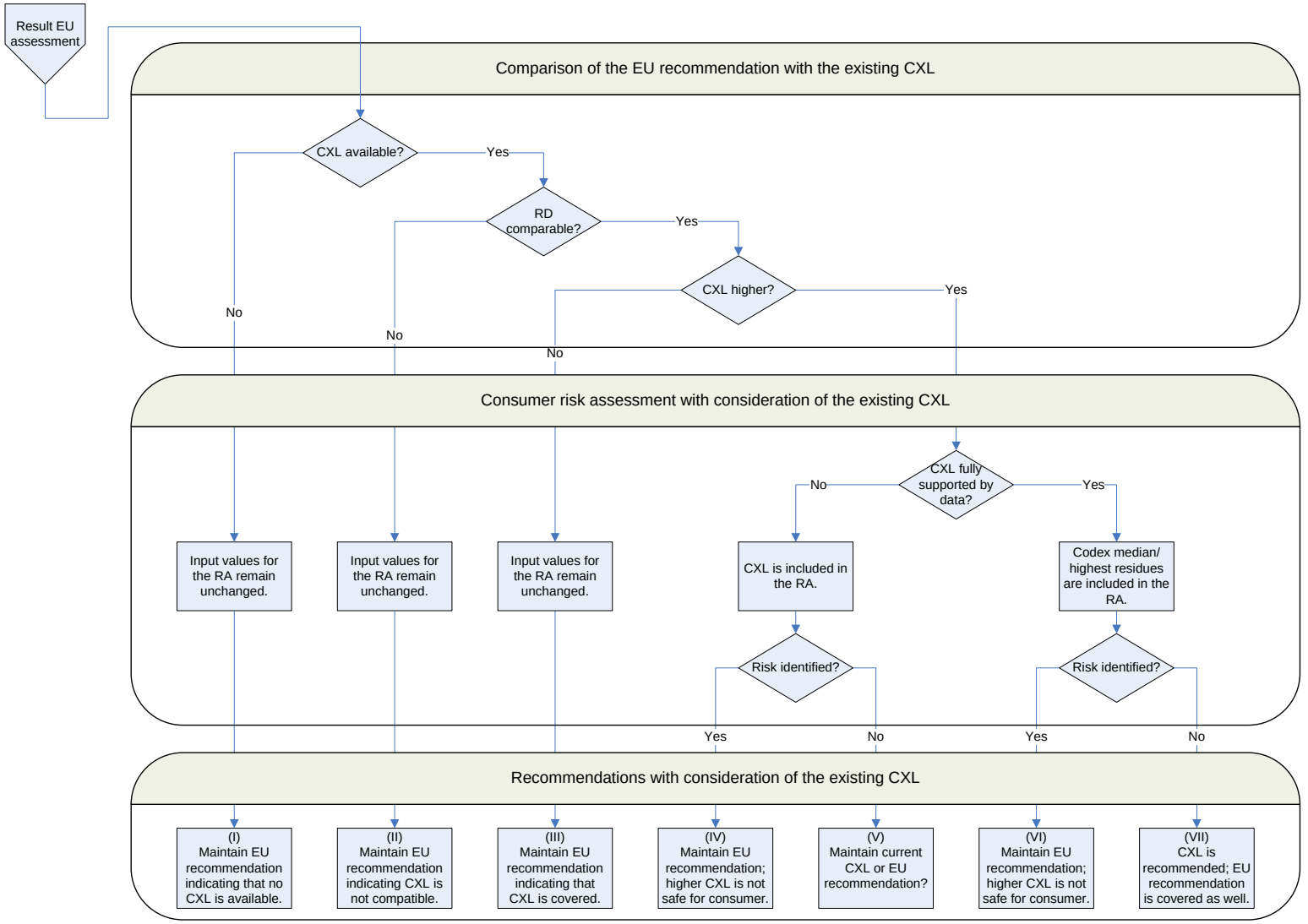
Code number	Groups and examples of individual products to which the MRLs apply (a)	Trinexapac
231010	Tomatoes (Cherry tomatoes,)	1
231020	Peppers (Chilli peppers)	1
231030	Aubergines (egg plants) (Pepino)	1
231040	Okra, lady's fingers	1
231990	Others	1
232000	(b) Cucurbits - edible peel	1
232010	Cucumbers	1
232020	Gherkins	1
232030	Courgettes (Summer squash, marrow (patisson))	1
232990	Others	1
233000	(c) Cucurbits-inedible peel	1
233010	Melons (Kiwano)	1
233020	Pumpkins (Winter squash)	1
233030	Watermelons	1
233990	Others	1
234000	(d) Sweet corn	1
239000	(e) Other fruiting vegetables	1
240000	(iv) Brassica vegetables	1
241000	(a) Flowering brassica	1
241010	Broccoli (Calabrese, Chinese broccoli, Broccoli raab)	1
241020	Cauliflower	1
241990	Others	1
242000	(b) Head brassica	1
242010	Brussels sprouts	1
242020	Head cabbage (Pointed head cabbage, red cabbage, savoy cabbage, white cabbage)	1
242990	Others	1
243000	(c) Leafy brassica	1
243010	Chinese cabbage (Indian (Chinese) mustard, pak choi, Chinese flat cabbage (tai goo choi), peking cabbage (pe-tsai), cow cabbage)	1
243020	Kale (Borecole (curly kale), collards)	1
243990	Others	1
244000	(d) Kohlrabi	1
250000	(v) Leaf vegetables & fresh herbs	1
251000	(a) Lettuce and other salad plants including Brassicacea	1
251010	Lamb´s lettuce (Italian cornsalad)	1
251020	Lettuce (Head lettuce, lollo rosso (cutting lettuce), iceberg lettuce, romaine (cos) lettuce)	1
251030	Scarole (broad-leaf endive) (Wild chicory, red-leaved chicory, radicchio, curld leave endive, sugar loaf)	1
251040	Cress	1
251050	Land cress	1
251060	Rocket, Rucola (Wild rocket)	1
251070	Red mustard	1
251080	Leaves and sprouts of Brassica spp (Mizuna)	1
251990	Others	1
252000	(b) Spinach & similar (leaves)	1
252010	Spinach (New Zealand spinach, turnip greens (turnip tops))	1
252020	Purslane (Winter purslane (miner's lettuce), garden purslane, common purslane, sorrel, glassworth)	1
252030	Beet leaves (chard) (Leaves of beetroot)	1
252990	Others	1
253000	(c) Vine leaves (grape leaves)	1
254000	(d) Water cress	1
255000	(e) Witloof	1
256000	(f) Herbs	1
256010	Chervil	1
256020	Chives	1
256030	Celery leaves (fennel leaves , Coriander leaves, dill leaves, Caraway leaves, lovage, angelica, sweet cisely and other Apiacea)	1
256040	Parsley	1
256050	Sage (Winter savory, summer savory,)	1
256060	Rosemary	1
256070	Thyme (marjoram, oregano)	1
256080	Basil (Balm leaves, mint, peppermint)	1
256090	Bay leaves (laurel)	1
256100	Tarragon (Hyssop)	1
256990	Others	1
260000	(vi) Legume vegetables (fresh)	1
260010	Beans (with pods) (Green bean (french beans, snap beans), scarlet runner bean, slicing bean, yardlong beans)	1
260020	Beans (without pods) (Broad beans, Flageolets, jack bean, lima bean, cowpea)	1
260030	Peas (with pods) (Mangetout (sugar peas))	1
260040	Peas (without pods) (Garden pea, green pea, chickpea)	1
260050	Lentils	1
260990	Others	1
270000	(vii) Stem vegetables (fresh)	1
270010	Asparagus	1
270020	Cardoons	1
270030	Celery	1
270040	Fennel	1
270050	Globe artichokes	1
270060	Leek	1
270070	Rhubarb	1
270080	Bamboo shoots	1
270090	Palm hearts	1
270990	Others	1
280000	(viii) Fungi	1
280010	Cultivated (Common mushroom, Oyster mushroom, Shi-take)	1
280020	Wild (Chanterelle, Truffle, Morel ,)	1
280990	Others	1
290000	(ix) Sea weeds	1
300000	3. PULSES, DRY	
300010	Beans (Broad beans, navy beans, flageolets, jack beans, lima beans, field beans, cowpeas)	10
300020	Lentils	0,05*
300030	Peas (Chickpeas, field peas, chickling vetch)	0,05*
300040	Lupins	0,05*
300990	Others	0,05*
400000	4. OILSEEDS AND OILFRUITS	
401000	(i) Oilseeds	
401010	Linseed	0,05*
401020	Peanuts	0,05*
401030	Poppy seed	0,05*
401040	Sesame seed	0,05*
401050	Sunflower seed	0,05*
401060	Rape seed (Bird rapeseed, turnip rape)	2
401070	Soya bean	0,05*
401080	Mustard seed	0,05*
401090	Cotton seed	0,05*
401100	Pumpkin seeds	0,05*
401110	Safflower	0,05*
401120	Borage	0,05*
401130	Gold of pleasure	0,05*
401140	Hempseed	0,05*
401150	Castor bean	0,05*
401990	Others	0,05*
402000	(ii) Oilfruits	0,05*
402010	Olives for oil production	0,05*
402020	Palm nuts (palmoil kernels)	0,05*
402030	Palmfruit	0,05*
402040	Kapok	0,05*
402990	Others	0,05*
500000	5. CEREALS	0,5
500010	Barley	0,5
500020	Buckwheat	0,5
500030	Maize	0,5
500040	Millet (Foxtail millet, teff)	0,5
500050	Oats	0,5
500060	Rice	0,5
500070	Rye	0,5
500080	Sorghum	0,5
500090	Wheat (Spelt Triticale)	0,5
500990	Others	0,5
600000	6. TEA, COFFEE, HERBAL INFUSIONS AND COCOA	0,05*
610000	(i) Tea (dried leaves and stalks, fermented or	0,05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Trinexapac
	otherwise of Camellia sinensis)	
620000	(ii) Coffee beans	0,05*
630000	(iii) Herbal infusions (dried)	0,05*
631000	(a) Flowers	0,05*
631010	Camomille flowers	0,05*
631020	Hybiscus flowers	0,05*
631030	Rose petals	0,05*
631040	Jasmine flowers	0,05*
631050	Lime (linden)	0,05*
631990	Others	0,05*
632000	(b) Leaves	0,05*
632010	Strawberry leaves	0,05*
632020	Rooibos leaves	0,05*
632030	Maté	0,05*
632990	Others	0,05*
633000	(c) Roots	0,05*
633010	Valerian root	0,05*
633020	Ginseng root	0,05*
633990	Others	0,05*
639000	(d) Other herbal infusions	0,05*
640000	(iv) Cocoa (fermented beans)	0,05*
650000	(v) Carob (st johns bread)	0,05*
700000	7. HOPS (dried) , including hop pellets and unconcentrated powder	0,05*
800000	8. SPICES	0,05*
810000	(i) Seeds	0,05*
810010	Anise	0,05*
810020	Black caraway	0,05*
810030	Celery seed (Lovage seed)	0,05*
810040	Coriander seed	0,05*
810050	Cumin seed	0,05*
810060	Dill seed	0,05*
810070	Fennel seed	0,05*
810080	Fenugreek	0,05*
810090	Nutmeg	0,05*
810990	Others	0,05*
820000	(ii) Fruits and berries	0,05*
820010	Allspice	0,05*
820020	Anise pepper (Japan pepper)	0,05*
820030	Caraway	0,05*
820040	Cardamom	0,05*
820050	Juniper berries	0,05*
820060	Pepper, black and white	0,05*
	(Long pepper, pink pepper)	
820070	Vanilla pods	0,05*
820080	Tamarind	0,05*
820990	Others	0,05*
830000	(iii) Bark	0,05*
830010	Cinnamon (Cassia)	0,05*
830990	Others	0,05*
840000	(iv) Roots or rhizome	0,05*
840010	Liquorice	0,05*
840020	Ginger	0,05*
840030	Turmeric (Curcuma)	0,05*
840040	Horseradish	0,05*
840990	Others	0,05*
850000	(v) Buds	0,05*
850010	Cloves	0,05*
850020	Capers	0,05*
850990	Others	0,05*
860000	(vi) Flower stigma	0,05*
860010	Saffron	0,05*
860990	Others	0,05*
870000	(vii) Aril	0,05*
870010	Mace	0,05*
870990	Others	0,05*
900000	9. SUGAR PLANTS	0,05*
900010	Sugar beet (root)	0,05*
900020	Sugar cane	0,05*
900030	Chicory roots	0,05*
900990	Others	0,05*
1000000	10. PRODUCTS OF ANIMAL ORIGIN- TERRESTRIAL ANIMALS	0,05*
1010000	(i) Meat, preparations of meat, offals, blood, animal fats fresh chilled or frozen, salted, in brine, dried or smoked or processed as flours or meals other processed products such as sausages and food preparations based on these	0,05*
1011000	(a) Swine	0,05*
1011010	Meat	0,05*
1011020	Fat free of lean meat	0,05*
1011030	Liver	0,05*
1011040	Kidney	0,05*
1011050	Edible offal	0,05*
1011990	Others	0,05*
1012000	(b) Bovine	0,05*
1012010	Meat	0,05*
1012020	Fat	0,05*
1012030	Liver	0,05*
1012040	Kidney	0,05*
1012050	Edible offal	0,05*
1012990	Others	0,05*
1013000	(c) Sheep	0,05*
1013010	Meat	0,05*
1013020	Fat	0,05*
1013030	Liver	0,05*
1013040	Kidney	0,05*
1013050	Edible offal	0,05*
1013990	Others	0,05*
1014000	(d) Goat	0,05*
1014010	Meat	0,05*
1014020	Fat	0,05*
1014030	Liver	0,05*
1014040	Kidney	0,05*
1014050	Edible offal	0,05*
1014990	Others	0,05*
1015000	(e) Horses, asses, mules or hinnies	0,05*
1015010	Meat	0,05*
1015020	Fat	0,05*
1015030	Liver	0,05*
1015040	Kidney	0,05*
1015050	Edible offal	0,05*
1015990	Others	0,05*
1016000	(f) Poultry -chicken, geese, duck, turkey and Guinea fowl-, ostrich, pigeon	0,05*
1016010	Meat	0,05*
1016020	Fat	0,05*
1016030	Liver	0,05*
1016040	Kidney	0,05*
1016050	Edible offal	0,05*
1016990	Others	0,05*
1017000	(g) Other farm animals (Rabbit, Kangaroo)	0,05*
1017010	Meat	0,05*
1017020	Fat	0,05*
1017030	Liver	0,05*
1017040	Kidney	0,05*
1017050	Edible offal	0,05*
1017990	Others	0,05*
1020000	(ii) Milk and cream, not concentrated, nor containing added sugar or sweetening matter, butter and other fats derived from milk, cheese and curd	
1020010	Cattle	0,05*
1020020	Sheep	0,05*
1020030	Goat	0,05*
1020040	Horse	0,05*
1020990	Others	0,05*
1030000	(iii) Birds' eggs, fresh preserved or cooked Shelled eggs and egg yolks fresh, dried, cooked by steaming or boiling in water, moulded, frozen or otherwise preserved whether or not containing added sugar or sweetening matter	0,05*
1030010	Chicken	0,05*
1030020	Duck	0,05*
1030030	Goose	0,05*
1030040	Quail	0,05*
1030990	Others	0,05*
1040000	(iv) Honey (Royal jelly, pollen)	
1050000	(v) Amphibians and reptiles (Frog legs, crocodiles)	
1060000	(vi) Snails	
1070000	(vii) Other terrestrial animal products	

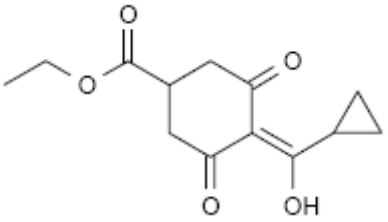
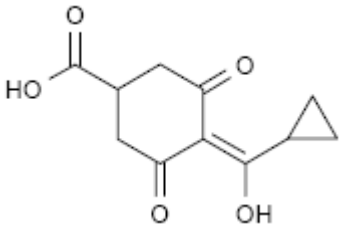
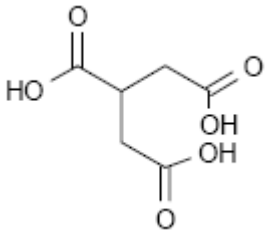
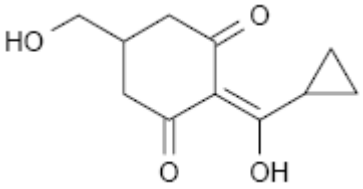
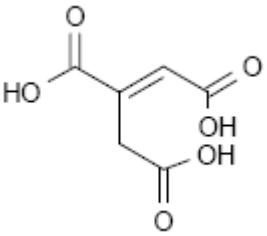
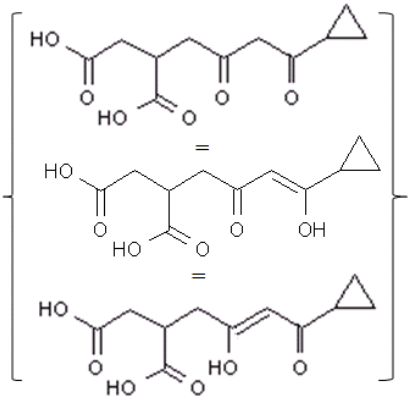
(*) Indicates lower limit of analytical determination
(a) Value voted by the Standing Committee on the Food Chain and Animal Health in June 2009 but not yet legally implemente

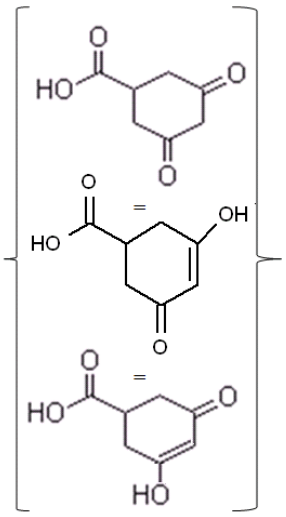
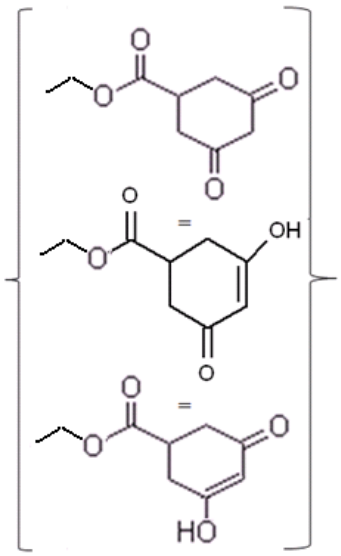
APPENDIX D – DECISION TREE FOR DERIVING MRL RECOMMENDATIONS




Result EU assessment
Comparison of the EU recommendation with the existing CXL
CXL available?
Yes
No
RD comparable?
Yes
No
CXL higher?
Yes
No
Consumer risk assessment with consideration of the existing CXL
CXL fully supported by data?
No
Yes
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
Input values for the RA remain unchanged.
CXL is included in the RA.
Codex median/ highest residues are included in the RA.
Risk identified?
Risk identified?
Yes
No
Yes
No
Recommendations with consideration of the existing CXL
(I) Maintain EU recommendation indicating that no CXL is available.
(II) Maintain EU recommendation indicating CXL is not compatible.
(III) Maintain EU recommendation indicating that CXL is covered.
(IV) Maintain EU recommendation; higher CXL is not safe for consumer.
(V) Maintain current CXL or EU recommendation?
(VI) Maintain EU recommendation; higher CXL is not safe for consumer.
(VII) CXL is recommended; EU recommendation is covered as well.

APPENDIX E – LIST OF METABOLITES AND RELATED STRUCTURAL FORMULA

Common name	IUPAC name	Structural formula
CGA 163935 (Trinexapac-ethyl)	4-(Cyclopropyl-alpha-hydroxy-methylene - 3,5-dioxocyclohexanecarboxylic acid ethylester	
CGA 179500 (Trinexapac)	4-(Cyclopropyl-alpha-hydroxy-methylene - 3,5-dioxocyclohexanecarboxylic acid	
CGA 275537	1,2,3-propanetricarboxylic acid (tricarballylic acid)	
CGA 351210	4-(cyclopropyl-alpha-hydroxy-methylene)- 3,5-dioxocyclohexane methanol	
CGA 312753	12,3-propene tricarboxylic acid (trans aconitic acid)	
CGA 313458	(2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid) or 3-carboxy-7-cyclopropyl-5,7-diketo-heptanoic acid	 keto-enol tautomerism

CGA 113745	3,5-dioxocyclohexanecarboxylic acid	 keto-enol tautomerism
CGA 158377	3,5-dioxocyclohexanecarboxylic acid ethylester	 keto-enol tautomerism

ABBREVIATIONS

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement residue definition to risk assessment residue definition
CXL	codex maximum residue limit
d	day
DAR	Draft Assessment Report (prepared under Council Directive 91/414/EEC)
DAT	days after treatment
DM	dry matter
DT_{90}	period required for 90 percent dissipation (define method of estimation)
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
GAP	good agricultural practice
ha	hectare
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
ILV	independent laboratory validation
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
L	litre
LOQ	limit of quantification
MRL	maximum residue limit

MS	Member States
NEU	northern European Union
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
PROFile	(EFSA) Pesticides Residues Overview File
R_{ber}	statistical calculation of the MRL by using a non-parametric method
R_{max}	statistical calculation of the MRL by using a parametric method
RA	risk assessment
RAC	raw agricultural commodity
RMS	rapporteur Member State
SEU	southern European Union
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organisation